

PSJ2 Exh 104

File Provided Natively



The image shows the header section of the Endo Pharmaceuticals website. At the top left is the Endo logo with the word "ENDO" in a bold, sans-serif font and "PHARMACEUTICALS" in smaller letters below it. The main title "ENDO PHARMACEUTICALS" is centered in a large, white, sans-serif font. Below the title is a horizontal collage of five images: a surgeon in an operating room, a group of people looking at a monitor, a close-up of a hand, and a group of professionals clapping. A dark blue banner at the bottom contains the text "breakthrough thinking. collaboration. customer focus. accountability." in a white, sans-serif font. Below the banner, the event details are listed: "Awakening to REMS... A New Reality in Pain Management", "R&D Lunch & Learn", and "November 15, 2011".

ENDO PHARMACEUTICALS

breakthrough thinking. collaboration. customer focus. accountability.

Awakening to REMS... A New Reality in Pain Management
R&D Lunch & Learn
November 15, 2011

breakthrough thinking. collaboration. customer focus. accountability.

AGENDA



- What is REMS- *Tara Chapman*
- Endo's FDA-approved Risk Minimization Activities- *Mark Collins*
- Public Health Issue Associated with Opioid Use- *Nancy Santilli*
- REMS Education & Resources- *Linda Kitlinski*
- Q & A

CONFIDENTIAL – Internal Use Only.

breakthrough thinking. collaboration. customer focus. accountability.

WHAT IS REMS?

- REMS – RISK EVALUATION AND MITIGATION STRATEGY
- REMS are part of certain drug and biologics applications to ensure the benefits of the drug (NDA/ANDA) or biologic (BLA) would outweigh the risks.
- The FDA may require that a REMS include elements that are necessary to assure safe use of the drug/biologic because of its inherent toxicity or potential harmfulness, if it is determined that:
 - The drug/biologic is shown to be effective but is associated with a serious adverse drug experience. The REMS is strategy to mitigate specific serious risk listed in the labeling for the drug/biologic
 - FDA is also authorized to require sponsors of approved applications without a REMS to submit a proposed REMS if the FDA becomes aware of new safety information

3

breakthrough thinking. collaboration. customer focus. accountability.

REMS BACKGROUND

- FDAAA – FOOD AND DRUG ADMINISTRATION AMENDMENTS ACT OF 2007
 - Signed into Law September 27, 2007
- To ensure industry compliance regarding REMS, civil money penalties can be applied for sponsor's violation to the requirement for a REMS
- The drug/biologic will be considered misbranded if the sponsor fails to comply with a requirement of the REMS.

CONFIDENTIAL– For Internal Use Only.

4

breakthrough thinking. collaboration. customer focus. accountability.

REMS VS. RISKMAP

- Required versus Recommended
- Content comparison using the Opana ER RiskMAP as an example
 - Submission of Assessments
 - Additional potential elements of the strategy (MedGuide and PPI)
 - Communication Plan
 - ETASU
 - Implementation System

CONFIDENTIAL— For Internal Use Only.

5

breakthrough thinking. collaboration. customer focus. accountability.

ENDO'S READINESS: CURRENT FDA-APPROVED RISK MINIMIZATION ACTIVITIES FOR ENDO'S PRODUCTS

- RiskMAP – the forerunner to REMS
- Several of our products have Medication Guides
 - Required if the FDA determines that the drug product is:
 1. one for which patient labeling could help **prevent** serious adverse effects
 2. one that has serious risk(s) (relative to benefits) of which patients should be made aware because information concerning the risk(s) could **affect patients' decision** to use, or to continue to use, the product
 3. important to health and patient adherence to directions for use is **crucial to the drug's effectiveness**

CONFIDENTIAL – For Internal Use Only.

6

Class/Product	Current FDA-approved Risk Minimization Activities			REMS in Prep?
	Med Guide (MG)	RiskMAP	REMS	
Antidepressants Amitriptyline HCl tablets Trazodone HCl tablets Venlafaxine HCl tablets	✓			
<i>Aveed*</i>	—	—	—	✓
Clonazepam tablets	✓		✓ (MG only)	
<i>Fentanyl generic*</i>	—	—	—	✓
Fortesta	✓			
NSAIDs	✓			
Levetiracetam tablets	✓		Not any more	
Metoclopramide tablets	✓		Not any more	
<i>Morphine sulfate ER</i>				✓
Mycophenolate	✓			✓
<i>Opana ER</i>		✓		✓
<i>Oxycodone HCl ER</i>				✓
Primidone tablets	✓		Not any more	
Propoxyphene(s)	✓		✓ (MG only)	
Voltaren Gel	✓			
Zolpidem tartrate tablets	✓		Not any more	
Totals	11	1	2	6 Products; 4 REMS

* Unapproved

CONFIDENTIAL – For Internal Use Only.

* Not including Patient Labeling (required for products containing estrogen)

ENDO'S READINESS: PARTICIPATION IN CLASS-WIDE REMS FOR PAIN PRODUCTS		
Products(s)	Opana ER Oxycodone HCl ER Morphine sulfate ER	Actiq generic (fentanyl)
Class	Long Acting / Extended Release (LAER) Opioids (21 Companies)	Transmucosal Immediate Release Fentanyl (TIRF) (10 Companies)
ETASUs	1. HCP training program 2. Patient education materials 3. HCP notification	1. HCPs specially certified 2. Specially certified pharmacies 3. Dispensed only with evidence of safe-use conditions
About the REMS program	The Sponsors will ensure that training is provided to healthcare providers who prescribe ER/LA opioids. The training will be conducted by accredited, independent continuing education (CE) providers , under educational grant provided by the Sponsors. Assessments of the effect of the CE program will be provided to the FDA.	Access to these medicines will be restricted to appropriately trained distributors, pharmacists, prescribers, and patients. Access requires successful completion of Knowledge Assessment . Entities re-enrolled every 2 years. Major assessments provided to the FDA: operational metrics of the REMS.
Expected REMS approval	Class REMS: February 2012 Interim REMS: December 2011	Class REMS: December 2011 Endo's ANDA: 4Q2012

CONFIDENTIAL – For Internal Use Only.

8

breakthrough thinking. collaboration. customer focus. accountability.

PUBLIC HEALTH ISSUE OF OPIOID USE

SUMMARY OF THE PUBLIC HEALTH CONUNDRUM

- Both undertreatment of pain & opioid abuse are significant Public Health issues
- ↑ Awareness of need to treat pain has ↑ opioid access & use
- ↑ Opioid access & use has ↑ availability of opioids for misuse
- Rx opioid-related deaths, addiction, abuse & misuse are on the rise
 - Increase has paralleled increase in Rx opioid sales
 - Teens & young adults are fastest growing groups
- > 70% of non-medical users of Rx pain relievers report friends or relatives as the source (2010 SAMHSA)
 - Awareness & educational interventions with prescribers, patients, public can have significant effects

CONFIDENTIAL— For Internal Use Only

9



breakthrough thinking. collaboration. customer focus. accountability.

RELATIONSHIP BETWEEN UNINTENTIONAL OD DEATHS AND SALES OF RX OPIOIDS.....A **DIRECT CORRELATION**

Unintentional Overdose Deaths Involving Opioid Analgesics Parallel Opioid Sales United States, 1997–2007

Distribution by drug companies

- 96 mg/person in 1997
- 698 mg/person in 2007
 - Enough for every American to take 5 mg Vicodin every 4 hrs for 3 weeks

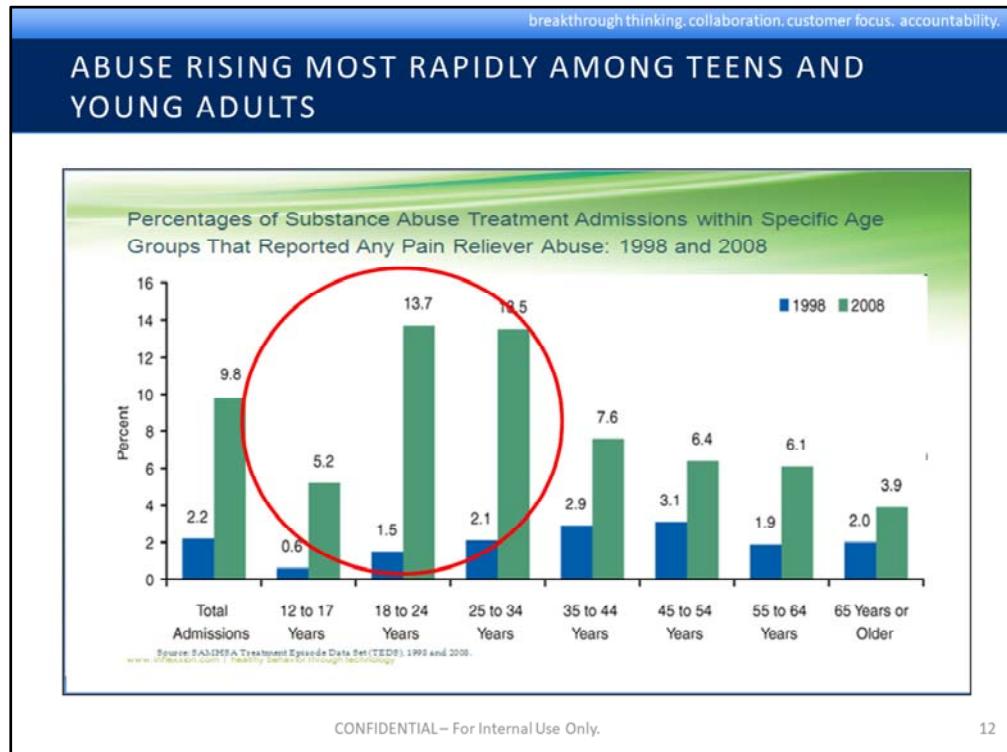
Overdose deaths

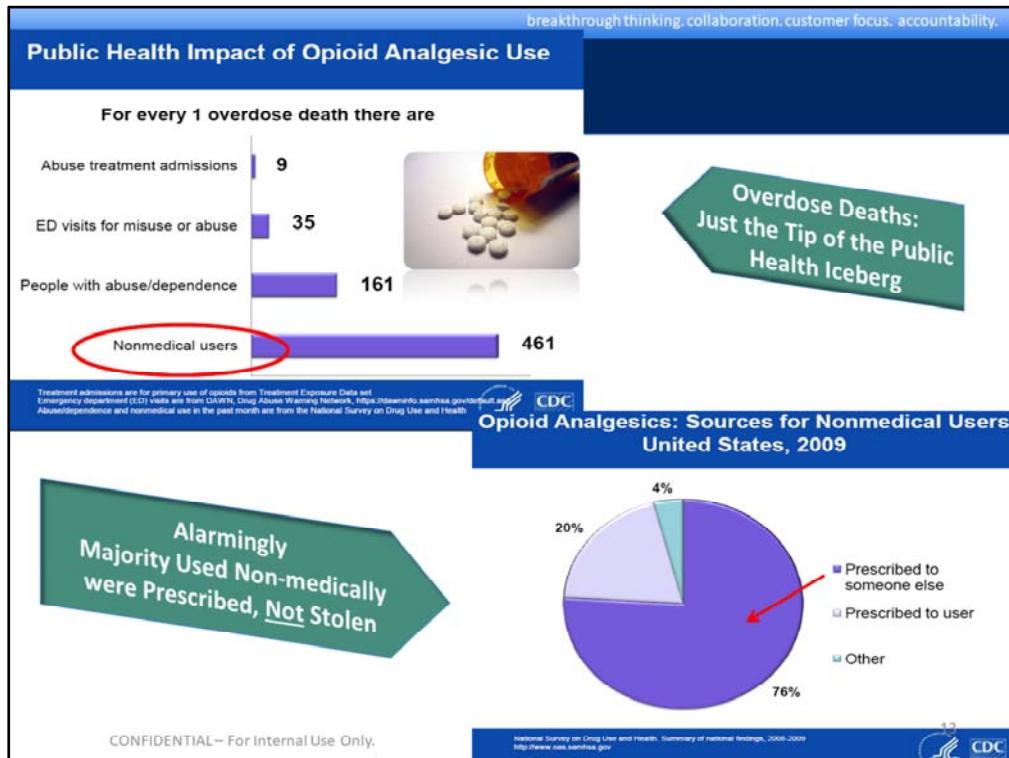
- 2,901 in 1999
- 11,499 in 2007

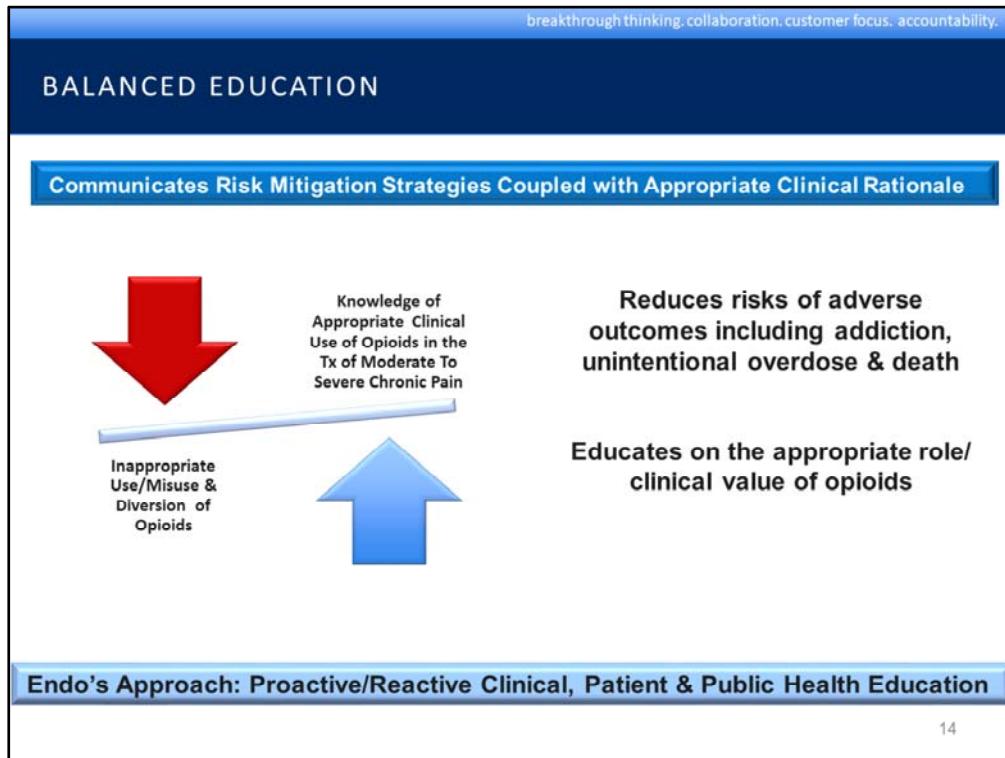
National Vital Statistics System, multiple cause of death data set and Drug Enforcement Administration ARCO System
* 2007 opioid sales figure is preliminary

CDC

10 CONFIDENTIAL – For Internal Use Only. 11







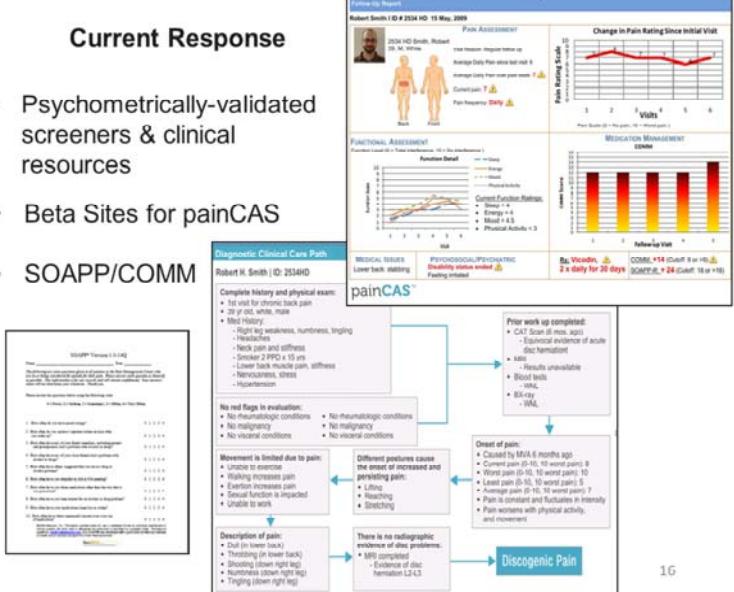
REMS EDUCATION VS "BALANCED" OPIOID EDUCATION (RISKMAP)	
<p>REMS Education</p> <ul style="list-style-type: none"> Education to be provided to LA/ER opioid Rx'ers <ul style="list-style-type: none"> CE-accredited Supported by IWG educational grants Focus will be on reducing risks of death, unintentional OD, addiction, abuse & serious AEs Minimal educational "outcomes" possible because of FDAA limitations Working closely with ACCME & FDA on: <ul style="list-style-type: none"> National database Standardized data fields & assessments Independent audits Metrics & timeline FDA released Draft Blueprint for CE on 11/7 <ul style="list-style-type: none"> One month public comment period 	<p>"Balanced" Opioid Education</p> <ul style="list-style-type: none"> Addresses both aspects of public health issue <ul style="list-style-type: none"> Responsible risk mitigation Appropriate dx & tx of chronic pain Discusses topics not covered by REMS <ul style="list-style-type: none"> Evidence-based guidelines Role of opioids in chronic pain Evolving research & data μ-opioid receptor variability Pain in the elderly Multimodal treatment approaches for <ul style="list-style-type: none"> LBP, OA, NP, etc. Educational outcomes to measure success All IWG Branded Companies (plus Covidien) plan to continue "balanced" education

CONFIDENTIAL – For Internal Use Only

15

breakthrough thinking. collaboration. customer focus. accountability.

PROBLEM IS MULTIFACTORIAL: RIGHT PATIENT... **RIGHT TREATMENT... PROPER FOLLOW-UP**

PROBLEM	Current Response
<p>Patient Assessment:</p> <ul style="list-style-type: none"> • Pain Intensity and Quality • Relative Risk of Addiction, Abuse, Misuse • Functionality <div style="text-align: center; margin-top: 10px;">  </div>	<p>Psychometrically-validated screeners & clinical resources</p> <ul style="list-style-type: none"> • Beta Sites for painCAS • SOAPP/COMM <div style="border: 1px solid black; padding: 10px; margin-top: 10px;">  <p>CONFIDENTIAL – For Internal Use Only</p> </div>

breakthrough thinking. collaboration. customer focus. accountability.

FACILITATION OF COORDINATED CARE IS CRITICAL ENDO AIMS TO DELIVER TOTAL SOLUTIONS

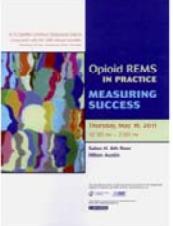
PROBLEM	Current Response
Appropriately Managing Chronic Pain Patients	<ul style="list-style-type: none">• Clinical Resources & Education<ul style="list-style-type: none">• PainEDU.com, painACTION.com, painCAS
Coordinated, Multidisciplinary Team Approach	<ul style="list-style-type: none">• Resident/Fellow Annual Training Program<ul style="list-style-type: none">• ~1000 trainees over 10 years• NIPC Live & Enduring• JAFP/NIPC Podcasts



CONFIDENTIAL – For Internal Use Only







17

breakthrough thinking. collaboration. customer focus. accountability.

OPIOID MISUSE, ABUSE & ADDICTION ARE SIGNIFICANT PUBLIC HEALTH ISSUES

PROBLEM



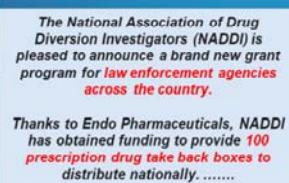
For every 1 overdose deaths there are

- ✓ 9 Abuse Tx admissions
- ✓ 35 ED visits for misuse or abuse
- ✓ 161 peoples with abuse/dependency
- ✓ 461 nonmedical users

Current Response

- Appropriate Prescribing Guidelines, Tools & Education
- Patient/Provider Agreements
- Safe Storage & Disposal Education
- Partnership for a Drug Free America Initiatives
- NADDI Pilot
- Take-Back Programs



CONFIDENTIAL – For Internal Use Only

18

breakthrough thinking. collaboration. customer focus. accountability.

ENDO SOLUTIONS TO YOUTH & YOUNG ADULT ABUSE/MISUSE/ADDICTION

PROBLEM	CURRENT RESPONSE
Rise in Teen and Young Adult Use 	<ul style="list-style-type: none"> Drugs4Real.com MyStudentBody.com National Association of School Nurses Symposium Partnership for a Drug-Free America Activities Support for Recovery High School Initiatives <p>Intervene If you witness or believe your child is developing an unhealthy interest in prescription drugs, call the Partnership for a Drug-Free America at 1-800-DRUGS-4-U (1-800-378-4738) or contact your local police or health department.</p> <p>Every day, 2500 teens abuse a prescription drug for the first time.</p>
 	

CONFIDENTIAL—For Internal Use

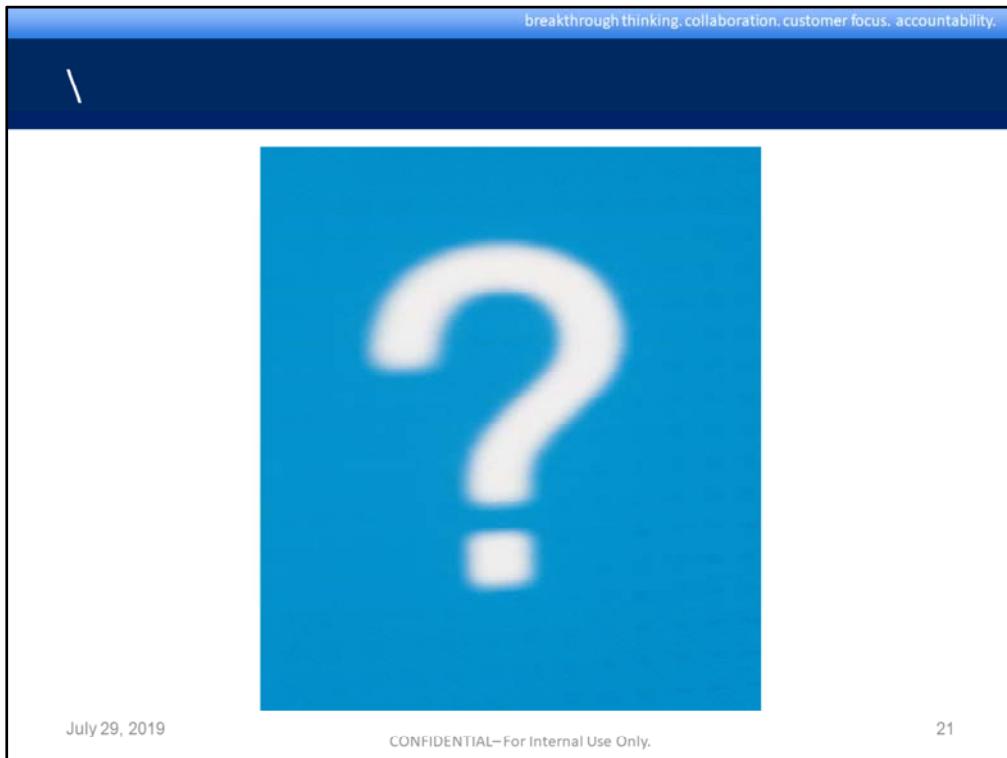
breakthrough thinking. collaboration. customer focus. accountability.

SUMMARY

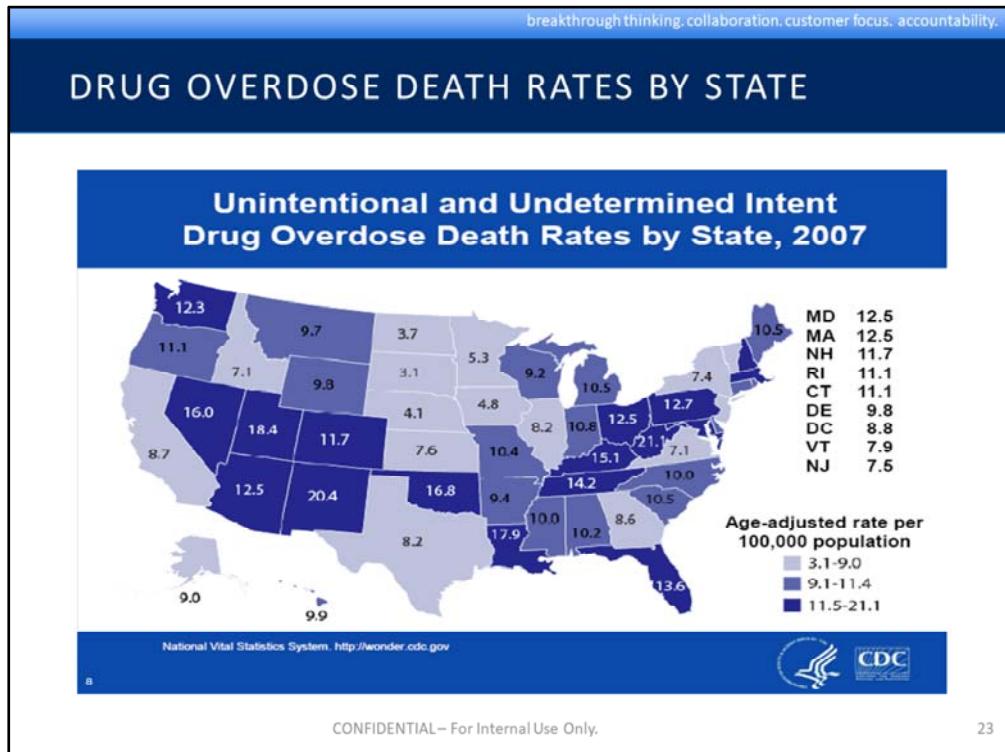
- Misuse & abuse of opioids is a major public health issue
 - Deaths from Rx opioids have reached epidemic levels
 - ~ 12 million Americans (age 12+) reported nonmedical use of Rx opioids in the past year
 - Impacting the problem requires concerted efforts of all stakeholders
- Endo has played a leadership role in IWG Activities
 - Selected as one of 3 major opioid mfgs on Steering Committee
 - Co-chair of Education Sub-team
 - Key roles in Regulatory, Metrics, Patient & Dispenser Sub-teams
 - Integrally involved in FDA/IWG response & negotiations
- Endo is well-positioned to respond to new REMS requirements
- Endo will continue to provide a balanced educational approach
 - Appropriate clinical use of opioids
 - Reduce risks of death, unintentional OD, addiction, misuse & abuse

CONFIDENTIAL—For Internal Use Only.

20







breakthrough thinking. collaboration. customer focus. accountability.

ENDO'S CURRENT PAIN ACTIVITIES: THE OPANA ER RISKMAP – GOALS AND OBJECTIVES

To minimize the following liabilities:

- Aberrant behavior such as drug abuse, misuse, and addiction
 - Among patients
 - In the community, particularly among young adults
- Unintentional drug overdose
- Accidental exposure
- Diversion from distribution/manufacturing facilities
- Improper patient selection
- Fraudulent prescription activity
- Inadequate patient education

CONFIDENTIAL – For Internal Use Only.

24

breakthrough thinking. collaboration. customer focus. accountability.

Endo: Differentiation & Leadership

- As branded & generic provider, uniquely positioned for REMS
- Long-standing leader & supporter of cutting-edge initiatives to support providers with abuse/misuse problem through the development of:

Awareness Activities

- Responsible Opioid Prescribing
- Drugs4Real.com
- Partnership for Drug Free America chart
- Opioid 911

Educational Resources

- Clinical Guide to Opioid Analgesia
- NIPC Live Regional & National Series
- Understanding Your Pain Brochure Series w/ JCAHO endorsement
- PainEdu site & Manual
- Primary Care Opioid Handbook
- MyStudentBody.com
- Veterans in Pain Initiatives (VIP)
- NIH Medline Plus Publication

Patient Management Tools

- SOAPP
- COMM
- painACTION
- painCAS
- PainSAFE
- Patient Action Steps Series
- APF & ACPA Resources

Community & Public Health

- NADDI Pilot
- NASCSA Initiatives
- DEA Takeback Activities
- National Association of School Nurses Education
- Drugs4Real.com

Continue to partner on innovative programs to lead community outreach efforts

CONFIDENTIAL – For Internal Use Only

25

NADDI take back pilot was brought up at a meeting on Tuesday by the Executive Director of NADDI (National Association of Drug Diversion Investigators). They are hoping to place mailbox type receptacles in police departments to serve as drop-off points for unneeded medications. Looking for a sponsor, Initial cost \$70K.

breakthrough thinking. collaboration. customer focus. accountability.

ENDO'S CURRENT PAIN ACTIVITIES: THE OPANA ER RISKMAP – TOOLS

- Product labeling
- Education
 - Professional education initiatives
 - Patient and family
 - Development of new clinically useful validated tools
 - Sales force training
- Tamper-resistant prescription pads
 - Discontinued
- Oversight of the distribution chain
- Postmarketing surveillance

CONFIDENTIAL – For Internal Use Only.

26